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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,355	07/06/2001	H. Craig Dees	PHO-122	5998

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EXAMINER	
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ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,355	DEES ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-11,19-22 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-11,19-22 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-07-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 102

2. Claims 1-3, 10, 19-22, and 27 remain rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al. for the reasons of record set forth in the prior Office Action mailed 2-18-04.

3. Applicant's arguments filed 8-20-04 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Williams et al. does not describe the claimed injectable solution, but rather is limited to topical gels, lotions, creams and ointments. Applicants argue that in all of the examples of Williams et al. the gel described is a topical preparation and is clearly not an intracorporeal pharmaceutical composition in a delivery vehicle consisting of a tablet, capsule, suppository or syrup, as recited in the claims of the present application. Moreover, Applicants argue that Williams et al. teaches away from the intracorporeal pharmaceutical compositions of the present invention, which consists of aqueous solutions, tablets, capsules, suppositories or syrups.

First it is noted that only claims 19-22 and 27 are limited to wherein the pharmaceutical compositions are formulated in a delivery vehicle consisting of an aqueous solution, a tablet, a capsule, a suppository or a syrup. Claims 1-4, and 9-11 are limited to compositions in an aqueous solution.

Contrary to Applicant's assertions, contemplates the photodynamic therapy comprising wherein photosensitising agents are administered by direct injection, see for example, col. 5, lines 33-40, which states: "[S]ensitizing agents used in the present invention are brought into contact with the vascular tissue in target lesions by topical application or direct injection into the target tissue. Such applications are intended to selectively sensitize the target lesion and avoid the adverse general light sensitivity found with conventional intravenous administration of sensitizing agents." See also claim 4 of the issued US Patent of Williams et al., which recites a method of photodynamic therapy wherein the photosensitizing agent is locally applied to target tissue by means of injecting said photosensitizing agent. In a preferred embodiment, the formulations of Williams et al. photosensitizing agents are formulation in an aqueous gel formulation (See col.).

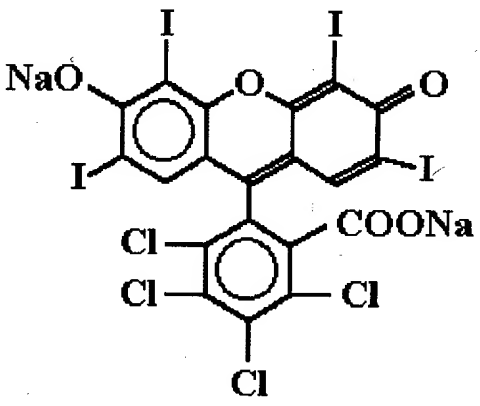
Therefore, contrary to Applicant's assertions, the disclosure of Williams et al. does not teach away from the injectable compositions recited in the instant claims.

4. Claims 1, 3-4, 19, and 21-22 remain rejected under 35 U.S.C. 102(b) as being anticipated by Goers et al. Claims 1-4, 9-11, 19-22 and 27 remain rejected under 35 U.S.C. 102(b) as being anticipated by Bottiroli et al. Claims 1, 3-4, 19, 21-22, remain rejected under 35 U.S.C. 102(b) as being anticipated by Schultz et al. Claims 2 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Goers et al. for the reasons of record set forth in the Official Action mailed 2-18-04.

Applicant's arguments filed 8-20-04 have been fully considered but they are not persuasive. Applicants traverse the above rejections on the grounds that Goers et al. teaches away from the claimed invention and a fundamental aspect of the present application, namely

that the halogenated xanthenes exhibit remarkable pharmacologic properties without requirement of exotic delivery formulations (such as liposomes) or antigeneic conjugates (such as antibody-agent conjugates). Additionally, Applicants argue that Goers fails to teach or suggest the presently claimed chemotherapeutic pharmaceutical compositions, consisting of sodium or potassium salts of the halogenated xanthenes, and further teaches away from such compositions by requiring compositions comprising "antibody therapeutic agent conjugates."

Contrary to Applicant's assertions, as stated in the prior Office Action, Applicants have not provided any evidence that the compounds disclosed by Goers et al. would not possess the same activity as the claimed compositions since the Goers et al. clearly state that photosensitizers, including in particular Rose Bengal (col. 20, lines 50-55), which is a disodium halogenated xanthene, and is further disclosed as being a therapeutic agent. Rose Bengal has the following structure:



Moreover, the presence of the antibody attachment to the photosensitizer agents of Goers et al., the photosensitizer is activated by a light source and its cytotoxic effect is mediated through the production of singlet oxygen, which results in toxicity to neighboring cells (col. 28, lines 45-68), this effect is not as a result of the antibody targeting moiety attachment. Moreover,

the photosensitizer compositions of Goers et al. are disclosed as being specific for tumor treatment (see col. 6, lines 22-28), and therefore can be considered a form of chemotherapeutic agent.

5. Applicants traverse the rejection over Bottiroli et al. on the grounds that Bottiroli et al. fails to teach or suggest the presently claimed chemotherapeutic pharmaceutical compositions, consisting of sodium or potassium salts of the halogenated xanthenes, and furthermore teaches away from such compositions by requiring compositions comprising "derivatives of xanthenes...containing quencher groups." According to Applicants Bottiroli et al. teaches that for any xanthene to have use in a pharmaceutical composition, it must be a specific derivative containing special fluorescence quencher groups. Contrary to Applicant's assertions Bottiroli et al. teaches that the quencher groups function to target the activity of the xanthene specifically to tumor cells, since the quencher groups are removed by specific enzyme activity found in tumor cells once the composition is taken up by the tumor cells. It remains that Bottiroli et al. clearly contemplate the treatment of tumors comprising the administration of compounds comprising the use of a halogenated xanthene (wherein Rose Bengal represents such a compound). Even when Rose Bengal is modified by an acetate group (See Page 4), there is still one sodium linked to the structure of the xanthene compound.

Additionally, although Bottiroli et al. teach "exotic" delivery formulations as asserted by Applicants, there is nothing in the instant claims that would suggest that these formulations are not encompassed by the instant claims which generically require a formulation comprising a sodium or potassium salt of a halogenated xanthene formulated in an aqueous solution, a tablet, a capsule, a suppository, or a syrup. Applicant have not provided any evidence that the

compositions of Bottiroli et al. would not have the same utility as applicant's claimed compositions.

Additionally, since Bottiroli et al. teach that halogenated xanthene containing pharmaceutical compositions can be used for the treatment of tumor, these compositions can also be considered a form of chemotherapeutic agent.

6. Applicants traverse the rejection over Schultz et al. on the grounds that the claims of the present application, excludes the conjugate agents disclosed in Schultz et al. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the recitation that conjugate agents are excluded from the instant claims) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

7. Schultz et al. disclose compositions comprising as a primary active functionality, a wide variety of fluoresces that may be employed either by themselves or in conjunction with quencher molecules as active functionalities. Contrary to Applicant's assertions, the fluorescers of Schultz et al. include xanthene (col. 9, line 66), and more specifically may include Rose Bengal (col. 10, line 26; which is known in the art to be a disodium modified halogenated xanthene).

Moreover, Applicants argue that Schultz et al. fails to teach the claimed chemotherapeutic pharmaceutical compositions since the xanthene compounds disclosed by Schultz et al. are used as reporter molecules and are not intended for use as chemotherapeutic agents. Contrary to Applicant's assertions, Schultz et al. disclose compositions comprising as a primary active functionality, a wide variety of fluoresces that may be employed either by

themselves or in conjunction with quencher molecules as active functionalities. In one particular embodiment, the fluorescers include xanthene (col. 9, line 66), and more specifically may include Rose Bengal (col. 10, line 26).

8. Applicant's arguments cannot take the place of evidence that the compositions disclosed by the cited references, particularly wherein the compositions comprise a halogenated xanthene, would not have the same functional activity as Applicant's claimed compositions. Therefore, absent evidence to the contrary the ordinary skilled artisan at the time of the instant invention would have expect that the compositions disclosed in the cited references would have the same functional activity as Applicant's compositions.

Applicant's arguments are not persuasive, the instant claims remain rejected for the reasons of record.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-4, 9-11, 19-22, and 27 are provisionally rejected under the judicially created 1-11 of copending Application No. 10/331,735. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are

drawn to intracoporeal or injectable chemotherapeutic or pharmaceutical compositions consisting of a sodium or potassium salt of a halogenated xanthene compound in an aqueous solution, and the claims of the co-pending application are similarly drawn to medicaments comprising at least one halogenated xanthene as a primary active component, wherein said medicament is useful for chemotherapeutic treatment of human and animal tissue. The invention recited in the claims of the instant application and the copending application 10/331,735, are both drawn to compositions or medicaments that contain a halogenated xanthene.

Although, the claims of the instant application recite sodium or potassium salts of a halogenated xanthene, it is noticed that the halogenated xanthene compounds recited in claim 4 of the copending applicant encompass wherein the halogenated xanthene compound is a sodium or potassium salt. For example, claims 3 and 4 of the copending application recite the sodium modified halogenated xanthene compound Rose Bengal, these claims render obvious the limitation in the instant claims requiring that the halogenated xanthene compound is a sodium or potassium salt.

Additionally, claim 11 of the copending application, which recites multiple modes of intracorporeal injection, renders obvious the limitation in the instant claims requiring that the claimed compositions are injectable or useful for intracorporeal administration.

One of skill in the art at the time of the instant invention would have recognized that the photodynamic medicaments and pharmaceutical compositions of the copending application also encompasses the injectable or intracorporeal administered halogenated xanthene compositions for chemotherapeutic treatment, of the instant application.

Therefore, the claims of the co-pending application represent an obvious variation of the claims in the instant application. See MPEP § 804, which states that "[T]hose portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent."

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

JLE